



Aloe Vera

Updated: May 24, 2022.

OVERVIEW

Introduction

Aloe vera is a cactus-like plant belonging to the Lily family, extracts of which are used topically for skin care and orally as a component of many herbal mixtures claimed to have medicinal benefits. Oral forms of aloe vera have been linked to rare instances of clinically apparent liver injury.

Background

Aloe vera (“true, shining bitter substance”) is derived from a cactus-like plant, a member of the Lily family that grows best in arid climates. Aloe vera has been used for centuries for its purported healing properties. Aloe vera products are derived from the leaf (either the gel or leaf rind latex) and contain over 75 identified substances including anthraquinones (phenolic compounds with laxative actions), vitamins (A, C, E), enzymes (alialase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulose, lipase, and peroxidase), minerals, sugars, fatty acids, amino acids, salicylic acid and hormones (auxins and gibberellins suspected to have antiinflammatory activity). Aloe creams are found in hundreds of skin products used for cosmetic purposes and wound healing. Extracts and powdered extracts from leaf rind latex of aloe vera are used in small amounts as a food flavoring and in larger amounts in dietary supplements. In addition, aloe vera is claimed to have beneficial effects on arthritis, asthma, chronic fatigue, dyspepsia, constipation and various skin ailments. Recently, it has also been claimed to be helpful in weight loss. The bases of these claims have not been substantiated, but in vitro and animal studies suggest that components of aloe vera have antiproliferative, antiinflammatory, and hepato-protective properties. Aloe vera is generally tolerated without adverse events; minor side effects may include diarrhea, abdominal discomfort and nausea. Chronic use for constipation can lead to discoloration of the colon (pseudo-melanosis coli). Rare instances of hypersensitivity reactions, skin rash and allergic dermatitis have been described.

Hepatotoxicity

Liver injury attributable to oral preparations of aloe vera was first reported in 2005 and at least a dozen cases of clinically apparent liver injury have been published or mentioned in the literature. The injury typically arises between 3 and 24 weeks after starting oral aloe vera, usually provided in high doses to treat constipation, dyspepsia, aging, weight loss or to improve wellness. The typical pattern of injury is hepatocellular and the clinical course resembles acute viral hepatitis (Case 1). Immunoallergic and autoimmune features are rare. Liver biopsy shows changes typical of hepatitis with spotty cell injury and lobular and portal inflammation. The injury is rarely severe and fatal cases have not been reported.

Likelihood score: B (likely but rare cause of clinically apparent liver injury).

Mechanism of Injury

Aloe vera leaf extracts have many components, but none of them has been shown to be particularly hepatotoxic. The rare cases of liver injury reported with aloe vera use have had idiosyncratic features.

Outcome and Management

Hepatotoxicity from aloe vera is rare and cases have been self-limiting upon stopping the herbal. While some reported cases have been severe or prolonged, there have been no instances leading to fatalities, liver transplantation, chronic hepatitis, or vanishing bile duct syndrome. Rechallenge has led to recurrence of injury in at least one published case report (Case 2) and should be avoided.

Drug Class: [Herbal and Dietary Supplements](#)

CASE REPORTS

Case 1. Acute hepatitis due to aloe vera extract.(1)

A 57 year old German woman developed jaundice, itching and right upper quadrant pain 3 to 4 weeks after starting aloe vera tablets (500 mg daily), which she was taking for aging. She also was taking vitamin C and zinc, but no other prescription medications. She denied a history of liver disease, alcohol use or risk factors for viral hepatitis. On examination, she was jaundiced and had right upper quadrant tenderness, but no rash, fever or signs of chronic liver disease. Laboratory testing showed increased bilirubin values (8.9 mg/dL) and marked elevations in serum aminotransferase levels (ALT 1480 U/L, AST 711 U/L), with minimal increase in alkaline phosphatase (265 U/L) (Table). Tests for acute hepatitis A, B, C and E were negative. Serum antinuclear antibody was borderline positive (titer 1:40). Abdominal ultrasound showed no evidence of biliary obstruction. A liver biopsy showed an acute hepatitis, with portal and parenchymal infiltrates including plasma cells and eosinophils and bridging necrosis with cholestasis. The aloe vera was stopped and her symptoms rapidly resolved. The biochemical abnormalities resolved more slowly; serum enzymes were still elevated 5 months later but were near normal at one year.

Key Points

Medication:	Aloe vera (500 mg daily)
Pattern:	Hepatocellular (R=39)
Severity:	3+ (jaundice, hospitalization)
Latency:	4 weeks
Recovery:	6 months
Other medications:	Vitamin C, zinc

Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
Aloe vera tablets 500 mg daily for 4 weeks					
4 weeks	0	1480	265	8.9	Admission, liver biopsy
6 weeks	2 weeks	226			Discharge
6 months	5 months	180		Normal	Asymptomatic
1 year	12 months	40		Normal	

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Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
Normal Values		<22	<160	<1.2	

Comment

This was the first published report of hepatitis from aloe vera. An elderly woman with no exposures to viral hepatitis or other reasons to have liver disease developed an acute hepatitis-like syndrome after taking an oral aloe vera extract for a month. Most other causes of acute hepatitis were adequately excluded. A liver biopsy showed an acute hepatitis with cholestasis and eosinophils suggestive of a drug induced liver injury. Biochemical recovery was somewhat prolonged. While there did not appear to be other possible causes for liver injury in this case, the issue of possible contamination is always present and the aloe vera product being used had been purchased outside of Germany.

Case 2. Recurrent acute hepatitis due to aloe vera.(2)

A 62 year old Korean woman developed fatigue followed by jaundice 3 months after starting an aloe vera powder (420 mg daily). There was no history of liver disease or alcoholism. Laboratory test results showed a serum total bilirubin of 14.6 mg/dL with marked elevations in serum aminotransferase levels (ALT 1564 U/L, AST 1477 U/L), but minimal increases in alkaline phosphatase (211 U/L) (Table). Tests for hepatitis A, B, C and E were negative. Abdominal ultrasound showed no evidence of biliary obstruction. A liver biopsy showed changes of acute hepatitis with lobular and portal infiltrates and cholestasis. The aloe vera was stopped and after a week she began to improve. Six weeks after stopping the herbal, liver tests were close to normal. During subsequent follow up, however, she restarted an aloe vera extract and a month later serum ALT values were again elevated (785 U/L), although bilirubin was normal. Six months later she returned with jaundice (bilirubin 15.8 mg/dL, ALT 1135 U/L, alkaline phosphatase 243 U/L), but refused admission or further evaluation.

Key Points

Medication:	Aloe vera (420 mg daily)
Pattern:	Hepatocellular (R=32)
Severity:	3+ (jaundice, hospitalization)
Latency:	3 months initially, 1 month on reexposure
Recovery:	Approximately 6 weeks; relapse on reexposure
Other medications:	None mentioned

Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
Aloe vera 420 mg daily for ~3 months					
12 weeks	0	1564	211	14.6	Admission
13 weeks	1 week	1504	202	21.2	Liver biopsy
14 weeks	2 weeks	754	176	5.8	
15 weeks	3 weeks	425	163	4.5	
16 weeks	4 weeks	135	110	3.4	
18 weeks	6 weeks	21	110	2.1	

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Time After Starting	Time After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
		Aloe vera 420 mg daily, restarted for 1 month			
4 weeks	0	785	165	1.5	
Normal Values		<33	<160	<1.2	

Comment

This is one of the better documented cases of acute liver injury due to an aloe vera product in the literature. The latency to onset was 3 months initially and the patient developed fairly severe jaundice. Serum aminotransferase levels were quite high and the pattern of injury was clearly hepatocellular. A week after the aloe vera was stopped, liver tests began to improve and they were almost normal 6 weeks later. This patient was an herbal salesperson and restarted the aloe vera on her own, despite having been told that it probably caused the liver injury. The latency on reexposure was only one month, although the injury was somewhat less severe, with enzyme elevations without jaundice. However, six months later she returned with jaundice and a similar pattern of serum enzyme elevations, but refused further evaluation. While recurrent toxic hepatitis due to reexposure was the most likely diagnosis, the other possibility was a relapsing, acute onset of autoimmune hepatitis.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Aloe Vera – Generic

DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

Fact Sheet at National Center for Complementary and Integrative Health, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Aloe Vera	8001-97-6	Herbal	Not Applicable

CITED REFERENCES

1. Rabe C, Musch A, Schirmacher P, Kruis W, Hoffmann R. Acute hepatitis induced by an aloe vera preparation: A case report. *World J Gastroenterol.* 2005;11:303–4. PubMed PMID: 15633238.
2. Yang HN, Kim DJ, Kim YM, Kim BH, Sohn KM, Choi MJ, Choi YH. Aloe-induced toxic hepatitis. *J Korean Med Sci.* 2010;25:492–5. PubMed PMID: 20191055.

ANNOTATED BIBLIOGRAPHY

References updated: 24 May 2022

- Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 731-4.
- (Expert review of hepatotoxicity published in 1999; several herbal medications are discussed, but not aloe vera).*
- Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 733-54.
- (Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; mentions that aloe vera is generally nonhepatotoxic).*
- Aloe. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 19-26.
- (Compilation of short monographs on herbal medications and dietary supplements).*
- Vogler BK, Ernst E. Aloe vera: a systematic review of its clinical effectiveness. Br J Gen Pract. 1999;49:823-8. PubMed PMID: 10885091.
- (Systematic review of the literature on aloe vera identified 3 controlled trials of oral therapy for short periods in hyperlipidemia and diabetes found only mild and reversible adverse events and no mention of hepatotoxicity).*
- Stedman C. Herbal hepatotoxicity. Semin Liver Dis. 2002;22:195-206. PubMed PMID: 12016550.
- (Review and description of patterns of liver injury due to herbals, including discussion of potential risk factors, and herb-drug interactions).*
- Luyckx VA, Ballantine R, Claeys M, Cuyckens F, Van den Heuvel H, Cimanga RK, Vlietinck AJ, et al. Herbal remedy-associated acute renal failure secondary to Cape aloes. Am J Kidney Dis. 2002;39:E13. PubMed PMID: 11877593.
- (47 year old man presented with acute renal failure and serum enzyme elevations [ALT 713 U/L, AST 2034 U/L, Alk P 74 U/L, bilirubin 0.6 mg/dL], having taken herbal medications for digestive complaints; mass spectrometry of herbal revealed it to be an extract of Aloe capensis).*
- Schiano TD. Hepatotoxicity and complementary and alternative medicines. Clin Liver Dis. 2003;7:453-73. PubMed PMID: 12879994.
- (Comprehensive review of herbal associated hepatotoxicity, including common patterns of presentation).*
- Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. Aliment Pharmacol Ther. 2003;18:451-71. PubMed PMID: 12950418.
- (Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series, most common agents being celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma huang [3], pennyroyal [1], skullcap [2], Chinese herbs [9], valerian [1]).*
- Estes JD, Stolpman D, Olyaei A, Corless CL, Ham JM, Schwartz JM, Orloff SL. High prevalence of potentially hepatotoxic herbal supplement use in patients with fulminant hepatic failure. Arch Surg. 2003;138:852-8. PubMed PMID: 12912743.
- (Among 20 patients undergoing liver transplantation for acute liver failure during 2001-2, 10 were potentially caused by herbals, but none attributed to aloe vera).*
- Langmead L, Feakins RM, Goldthorpe S, Holt H, Tsironi E, De Silva A, Jewell DP, et al. Randomized, double-blind, placebo-controlled trial of oral aloe vera gel for active ulcerative colitis. Aliment Pharmacol Ther. 2004;19:739-47. PubMed PMID: 15043514.

(Randomized controlled trial of 4 week course of aloe vera vs placebo in 44 patients with ulcerative colitis found improvements in clinical scores with aloe vera; adverse side effects were minor and similar in the two groups, and “no patient developed abnormal blood tests attributable to aloe vera”).

Can A, Akev N, Ozsoy N, Bolkent S, Arda BP, Yanardag R, Okyar A. Effect of aloe vera leaf gel and pulp extracts on the liver in type-II diabetic rat models. *Biol Pharm Bull.* 2004;27:694–8. PubMed PMID: 15133247.

(In animal models exposed to stress, aloe vera appeared to attenuate liver injury attributable to diabetes).

Rabe C, Musch A, Schirmacher P, Kruis W, Hoffmann R. Acute hepatitis induced by an aloe vera preparation: A case report. *World J Gastroenterol.* 2005;11:303–4. PubMed PMID: 15633238.

(57 year old German woman developed jaundice and itching 1 month after starting aloe vera [500 mg/day] [bilirubin 8.9 mg/dL, ALT 1480 U/L, Alk P 265 U/L], resolving slowly: Case 1).

Kanat O, Ozet A, Ataergin S. Aloe vera-induced acute toxic hepatitis in a healthy young man. *Eur J Intern Med.* 2006;17:589. PubMed PMID: 17142185.

(24 year old man developed jaundice 3 weeks after starting aloe vera [500 mg by mouth daily] [bilirubin 9 mg/dL, ALT 2400 U/L, Alk P 400 U/L], resolving within 6 weeks of stopping).

Bottenberg MM, Wall GC, Harvey RL, Habib S. Oral aloe vera-induced hepatitis. *Ann Pharmacother.* 2007;41:1740–3. PubMed PMID: 17726067.

(73 year old woman developed jaundice having taking aloe vera capsules for constipation for five years [bilirubin 10.7 rising to 22.8 mg/dL, ALT 1451 U/L, Alk P 328 U/L, SMA 1:160], with normal ERCP and liver biopsy showing acute hepatitis, resolving within 4 months of stopping).

Seeff LB. Herbal hepatotoxicity. *Clin Liver Dis.* 2007;11:577–96. PubMed PMID: 17723921.

(Review of herbal induced hepatotoxicity, with details on specific herbal compounds).

Chalasanani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. *Gastroenterology.* 2008;135:1924–34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, 9% of cases were attributed to herbal medications, but no case was attributed to aloe vera alone or in combination with other agents).

Belfrage B, Malmstrom R. *Lakartidningen.* 2008;105:45. [Several cases of liver affected by aloe vera]. Swedish. PubMed PMID: 18293747.

(Reports of liver injury due to aloe vera include 4 in the Swedish database [2 hepatitis, 1 jaundice and 1 enzyme elevations only, arising within 3 months after starting and resolving on stopping] and 5 in the international database [2 hepatitis and 3 with enzyme elevations only]).

Curciarello J, De Ortuzar S, Borzi S, Bosia D. *Gastroenterol Hepatol.* 2008;31:436–8. [Severe acute hepatitis associated with intake of aloe vera tea]. Spanish. PubMed PMID: 18783689.

(26 year old man developed abdominal pain followed by jaundice 4 weeks after starting homemade aloe vera tea [bilirubin 8.4 rising to 13.8 mg/dL, ALT 935 U/L, Alk P normal], with subsequent worsening of protime and appearance of ascites, resolving 4 months after tea was stopped).

Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. *Indian J Dermatol.* 2008;53:163–6. PubMed PMID: 19882025.

(Overview of the known contents and purported activities of aloe vera; clinical use is supported mostly by anecdotal data and results of clinical trials have been “mixed”; hepatitis listed as a side effect).

- García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. Rev Esp Enferm Dig. 2008;100:688–95. [Liver injury induced by "natural remedies": an analysis of cases submitted to the Spanish Liver Toxicity Registry]. Spanish. PubMed PMID: 19159172.
- (Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, none due to aloe vera).*
- Navarro VJ. Herbal and dietary supplement hepatotoxicity. Semin Liver Dis. 2009;29:373–82. PubMed PMID: 19826971.
- (Overview of the regulatory environment, clinical patterns, and future directions in research with HDS; aloe vera is listed as a potential hepatotoxin but not specifically discussed).*
- Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. Pharmacoepidemiol Drug Saf. 2009;18:1039–47. PubMed PMID: 19650152.
- (Review of 778 spontaneous reports of adverse reactions to herbals to Swedish Registry found 15 to Aloe vera, including two cases of hepatitis; no details given).*
- Yang HN, Kim DJ, Kim YM, Kim BH, Sohn KM, Choi MJ, Choi YH. Aloe-induced toxic hepatitis. J Korean Med Sci. 2010;25:492–5. PubMed PMID: 20191055.
- (Three women, ages 55 to 62 years, developed symptomatic liver injury 3 to 6 months after starting aloe vera extract [bilirubin 1.6, 14.6 and 0.8 mg/dL, ALT 565, 1564 and 666 U/L, Alk P 309, 211 and 298 U/L], resolving rapidly with stopping, one patient having recurrence upon reexposure: Case 2).*
- Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.
- (Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury of which 12 [9%] were due to herbals, including several herbal mixtures, usnic acid, Ma Huang, black cohosh, and Hydroxycut, but not aloe vera).*
- Stickel F, Kessebohm K, Weimann R, Seitz HK. Review of liver injury associated with dietary supplements. Liver Int. 2011;31:595–605. PubMed PMID: 21457433.
- (Review of current understanding of liver injury from herbals and dietary supplements focusing upon Herbalife and Hydroxycut products, green tea, usnic acid, noni juice, Chinese herbs, vitamin A and anabolic steroids; aloe vera is not discussed).*
- Jiménez-Encarnación E, Ríos G, Muñoz-Mirabal A, Vilá LM. Euforia-induced acute hepatitis in a patient with scleroderma. BMJ Case Rep 2012; 2012.
- (45 year old woman with systemic sclerosis developed jaundice 1 month after starting Euphoria, a combination herbal product whose ingredients included aloe vera, resveratrol, green tea, noni and several berries [bilirubin 17.7 mg/dL, ALT 837 U/L, Alk P 134 U/L], with slow recovery over the 18 months after stopping).*
- Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. Liver Int. 2012;32:1543–56. PubMed PMID: 22928722.
- (A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements including four publications on aloe vera).*
- Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation and outcomes in patients with drug-induced liver injury in the General population of Iceland. Gastroenterology. 2013;144:1419–25. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, 15 of which [16%] were attributed to HDS products, but none were listed as containing aloe vera).

Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther.* 2013;37:3–17. PubMed PMID: 23121117.

(Systematic review of literature on HDS associated liver injury mentions that aloe vera has been associated with clinically apparent hepatotoxicity).

Teschke R, Genthner A, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: analysis of cases with initially reported positive re-exposure tests. *Dig Liver Dis.* 2014;46:264–9. PubMed PMID: 24315480.

(Reanalysis of published cases of herbal hepatotoxicity found criteria for a positive rechallenge by the RUCAM system was met in only 21 of 34 cases reporting a positive rechallenge; one case of rechallenge with aloe vera was considered "highly probable" [Yang 2010]).

Vázquez-Fernández P, Garayoa-Roca A, Añón-Rodríguez R, Cabezas-Macián M, Serra-Desfilis MÁ, Mora-Miguel F. Aloe vera: Not always so beneficial in patients with chronic liver disease. *Rev Esp Enferm Dig.* 2013;105:434–5. PubMed PMID: 24206557.

(49 year old man with chronic hepatitis C and cirrhosis developed jaundice after starting aloe vera drinks for 10 days [bilirubin 21 mg/dL, ALT 93 U/L, Alk P 421 U/L], no mention of previous laboratory results or response to withdrawal of the herbal).

Navarro VJ, Seeff LB. Liver injury induced by herbal complementary and alternative medicine. *Clin Liver Dis.* 2013;17:715–35. PubMed PMID: 24099027.

(Review of the epidemiology, regulatory status, diagnosis, pathogenesis and causes of liver injury from herbal products with specific discussion of conjugated linoleic acid, ephedra, germander, green tea, usnic acid, flavocoxid, aloe vera, chaparral, greater celandine, black cohosh, comfrey, kava, skullcap, valerian, noni juice, pennyroyal and traditional herbal remedies).

Lee J, Lee MS, Nam KW. Acute toxic hepatitis caused by an aloe vera preparation in a young patient: a case report with a literature review. *Korean J Gastroenterol.* 2014;64:54–8. PubMed PMID: 25073673.

(21 year old Korean woman developed fever and abdominal pain 1 month after starting a Herbalife preparation of aloe vera [bilirubin 1.5 mg/dL, ALT 1703 U/L, Alk P 709 U/L, white count 850/uL, platelets 57,000/uL], resolving within a month of stopping; literature review found 8 cases, 6 women, average age 47 years, all hepatocellular, 5 with jaundice, all recovered and 1 with a positive rechallenge).

Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. *Hepatology.* 2014;60:1399–408. PubMed PMID: 25043597.

(Among 839 cases of liver injury from drugs collected in the US between 2004 and 2013, 130 were due to HDS products, including 45 from body building agents [probably anabolic steroids] and 85 from diverse HDS products including 1 linked with aloe vera in combination with 2 other agents).

Navarro VJ, Lucena MI. Hepatotoxicity induced by herbal and dietary supplements. *Semin Liver Dis.* 2014;34:172–93. PubMed PMID: 24879982.

(Review of the international regulatory framework for HDS products and the epidemiology, clinical presentation, diagnosis and cause of HDS associated liver injury with tables and discussion of the most commonly implicated agents, including aloe vera which has more than 75 different constituents and has been associated with acute hepatocellular injury with a male predominance, average age of 58 years and onset by 3 months; at least one case with a positive rechallenge has been described).

Rossi S, Navarro VJ. Herbs and liver injury: a clinical perspective. *Clin Gastroenterol Hepatol*. 2014;12:1069–76. PubMed PMID: 23924877.

(Review of frequency, diagnosis and causes of liver injury from herbal products discusses kava, black cohosh, pyrrolizidine alkaloids, flavocoxid, glucosamine, saw palmetto, green tea, usnic acid and several proprietary herbal mixtures but not aloe vera).

Zheng EX, Navarro VJ. Liver injury from herbal, dietary, and weight loss supplements: a review. *J Clin Transl Hepatol*. 2015;3:93–8. PubMed PMID: 26357638.

(Review of literature on liver injury attributed to herbal weight loss supplements, does not discuss aloe vera).

Seeff LB, Bonkovsky HL, Navarro VJ, Wang G. Herbal products and the liver: a review of adverse effects and mechanisms. *Gastroenterology*. 2015;148:517–532.e3. PubMed PMID: 25500423.

(Extensive review of herbal associated liver injury does not discuss aloe vera specifically).

Brown AC. Liver toxicity related to herbs and dietary supplements: Online table of case reports. Part 2 of 5 series. *Food Chem Toxicol*. 2017;107:472–501. PubMed PMID: 27402097.

(Description of an online compendium of cases of liver toxicity attributed to HDS products, lists at least 6 publications of case reports and case series implicating greater celandine in causing liver injury).

Parlati L, Voican CS, Perlemuter K, Perlemuter G. Aloe vera-induced acute liver injury: A case report and literature review. *Clin Res Hepatol Gastroenterol*. 2017;41:e39–e42. PubMed PMID: 27856182.

(68 year old Burkinabe woman was found to have abnormal liver tests but no symptoms of liver injury “several months” after starting aloe vera [ALT 196 U/L, GGT 196 U/L, bilirubin not given], which resolved within 8 weeks of stopping).

Hervás-García JV, Montané E, Serrado-Iglesias A, Ramo-Tello C. Toxic hepatitis after concomitant interferon beta and aloe vera treatment in a patient with multiple sclerosis. A case report. *Neurologia*. 2017;32:546–547. PubMed PMID: 26874569.

(61 year old woman with multiple sclerosis taking interferon beta-1a for 10 years and aloe vera for 3 years developed abdominal pain and fatigue and was found to have jaundice [bilirubin not given, ALT 824 U/L, Alk P 121], with rapid improvement on stopping and normal liver tests 6 months later).

Ghorbani A, Zarvandi M, Rakhshandeh H. A randomized controlled trial of a herbal compound for improving metabolic parameters in diabetic patients with uncontrolled dyslipidemia. *Endocr Metab Immune Disord Drug Targets*. 2019;19:1075–1082. PubMed PMID: 30727929.

(Among 50 patients with diabetes and dyslipidemia treated with a multiingredient herbal supplement [with aloe vera, fenugreek, black seed, psyllium, garlic and milk thistle] or placebo twice daily for 12 weeks, cholesterol, triglycerides, and HgA1c levels improved, and there was “no unwarranted effect” on serum creatinine, ALT or AST).

Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, et al; Spanish DILI Registry. Herbal and dietary supplement-induced liver injuries in the Spanish DILI Registry. *Clin Gastroenterol Hepatol*. 2018;16:1495–1502. PubMed PMID: 29307848.

(Among 856 cases of hepatotoxicity enrolled in the Spanish DILI Registry between 1994 and 2016, 32 were attributed to herbal products, the most frequent cause being green tea [n=8] and Herbalife products [n=6], while none were attributed to Aloe vera).

Bessone F, García-Cortés M, Medina-Caliz I, Hernandez N, Parana R, Mendizabal M, Schinoni MI, et al. Herbal and dietary supplements-induced liver injury in Latin America: experience from the LATINDILI Network. *Clin Gastroenterol Hepatol*. 2022;20(3):e548–e563. PubMed PMID: 33434654.

(Among 367 cases of hepatotoxicity enrolled in the Latin American DILI Network between 2011 and 2019, 29 [8%] were attributed to herbal products, the most frequent being green tea [n=7], Herbalife products [n=5] and garcinia [n=3], while none were attributed to aloe vera).

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J. Herb-induced liver injury: Systematic review and meta-analysis. *World J Clin Cases.* 2021;9:5490–5513. PubMed PMID: 34307603.

(Systematic review of the literature on herb induced liver injury identified 446 references describing 936 cases due to 79 different herbal products, the most common being He Shou Wu [91], green tea [90] Herbalife products [64], kava kava [62 and greater celandine [48]; there were 22 cases attributed to aloe vera which were usually mostly from Korea, Spain and the US, mostly hepatocellular [90%], with death in 10%, chronicity in 5% and recovery in 86% of cases).